What's New in Clinical Development Practices & Regulations Quarter 2 – 2024

EU REGULATION, GUIDELINES & INITIATIVES

EC – Four Summary Fact Sheets

In April 2023, the EC announced the proposal to reform the EU pharmaceutical legislations by revising and replacing the existing general pharmaceutical legislation (Regulation 726/2004 and Directive 2001/83/EC) and the legislation on medicines for children and for rare diseases (Regulation 1901/2006 and Regulation 141/2000/EC, respectively).

The aim of the proposal is to give the EU a competitive edge whilst maintain its high standards for quality and safety and at the same time tackling ongoing issues.

Four fact sheets have been issued to summarise EU's current challenges and proposals:

- Steering innovation to address unmet medical needs *factsheet_umn_en.pdf (europa.eu)*
- Addressing shortages of medicines and ensuring security of supply *factsheet_shortage-management_en.pdf (europa.eu)*
- Access to medicines in all Member States *factsheet_market-launch_en.pdf (europa.eu)*
- Incentives to steer innovation and achieve public health objectives *factsheet_rdp_en.pdf (europa.eu)*

On 11 April 2024, Members of the European Parliament voted to adopt the proposal. *Parliament adopts its position on EU pharmaceutical reform | News | European Parliament (europa.eu)*

However, the European Federation of Pharmaceutical Industries and Associations (EFPIA) believes that, despite various enhancements, the revisions will not meet the proposal's aim. *EFPIA responds to the European Parliament plenary vote: Despite improvements, the Pharmaceutical Legislation has a long way to go to restore Europe's competitive edge*

EU Clinical Trial Regulation (CTR) and Clinical Trials Information System (CTIS)

During the EMA Management Board Meeting on 21 March 2024, it was stressed that the 3-year transition period, which began when the CTR became applicable, ends on 30 January 2025. *About the clinical trials website - EMA (euclinicaltrials.eu): Transition Period*

- The revised transparency rule for CTIS will become applicable on 18 June 2024, when the technical updates for the system have been implemented. *Revised transparency rules for the EU Clinical Trials Information System (CTIS) | European Medicines Agency (europa.eu)*

On the 01 March 2024, version 6.8 of the Q&A was published. *regulation5362014_qa_en_0.pdf (europa.eu)*

Health Technology Assessment Regulation (HTAR): (EU) 2021/2282

The HTAR, which comes into effect in January 2025, will govern European cooperation on health technology assessment (HTA) for medicinal products and certain medical devices. *Regulation - 2021/2282 - EN - EUR-Lex (europa.eu)*

Recommendations to Strengthen Supply Chains of Critical Medicines

Recommendations by EMA's Medicines Shortages Steering Group (MSSG), will facilitate the availability and supply of critical human medicines for which vulnerabilities in the supply chain have been identified. *New recommendations to strengthen supply chains of critical medicines | European Medicines Agency (europa.eu)*

One Health – A European Joint Framework

On the 07 May 2024, five European agencies published the One Health joint framework, which aims to strengthen cooperation and make the EU and its Member States better equipped to prevent, predict, detect and respond to health threats. *One Health: a joint framework for action published by five EU agencies | European Medicines Agency (europa.eu)*

EMA - New Guideline on Non-Inferiority and Equivalence Comparisons Trials

The EMA has issued a new draft guideline on Sponsors' use of non-inferiority designs to assess the safety and effectiveness of new drugs in clinical trials. Comments are due by 31 May 2024 and EMA plans to release the draft guideline in October 2024. *concept-paper-development-guideline-non-inferiority-equivalence-comparisons-clinical-trials_en.pdf (europa.eu)*

The current guidelines, detailed below, will become obsolete as they are amalgamated into the new guideline.

- Guideline on the choice of Non-Inferiority Margin (2005)
- Points to Consider on Switching between Superiority and Non-Inferiority (2000)

EMA - Revised Guideline

This guideline on the environmental risk assessment of medicinal products for human use comes into effect 01 September 2024. *guideline-environmental-risk-assessment-medicinal-products-human-use-revision-1_en.pdf (europa.eu)*

EC - Boost to EU Biotechnology and Biomanufacturing

On 21 March 2024, the EC issued a communication paper which identifies the challenges to long-term competitiveness for biotechnology and biomanufacturing in the EU and suggests solutions on how to address these challenges. *ec_communication-biotechnology-biomanufacturing.pdf (europa.eu)*

Medical Device Coordination Group (MDCG)

Clinical Investigational Plan (CIP) Guidance - The EU Medical Device Regulation requires clinical device studies to follow an appropriate CIP which reflects the latest scientific and technical knowledge. *mdcg_2024-3_en_0.pdf (europa.eu)*

Investigator's Brochures (IB) for medical device studies – This MDCG guidance will assist medical device manufacturers to submit the necessary documentation to support clinical investigations that are part of a IB. *MDCG issues guidance on Investigator's Brochure for medical device studies | RAPS*

UK INITIATIVES AND GUIDELINES

ICH Guidelines Applicable to the UK

The Medicines and Healthcare products Regulatory Agency (MHRA) has published an online directory of the ICH guidelines that are applicable to the UK. *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guidelines - GOV.UK (www.gov.uk)*

Transparency and Data Sharing

As part of the Health Research Authority's (HRA's) transparency initiative, a list of the clinical trials that, in 2022, received a favourable opinion from a Research Ethics Committee (REC) has been published. *Clinical trial registration report 2022 - Health Research Authority (hra.nhs.uk)*

The British Medical Journal (*BMJ*) has introduced a new policy that requires its authors to share the clinical trial data and analytical code. This increases transparency, but also encourages scrutinization and thus enforcing quality. *Mandatory data and code sharing for research published by The BMJ | The BMJ*

Patient Advisory Council Report

In February 2024, the Association of the British Pharmaceutical Industry (ABPI) published a report on how to accelerate and enhance initiatives to make sure patients get faster, more equitable access to innovative treatments. *ABPI Patient Advisory Council Report*

MHRA Clinical Trial Authorisation (CTA) Applications

Applications for marketing authorisations for established medicines, submitted before 1 January 2024 which await the first assessment, may now convert to the agency's new Mutual Recognition and Decentralised Reliance Procedure or the European Commission Decision Reliance Procedure. *Established medicines: marketing authorisation application changes - GOV.UK (www.gov.uk)*

The MHRA reports:

- Latest performance data (for clinical trials September 2023 to February 2024 and clinical investigations March 2023 to February 2024) show that CTA applications continue to be handled within the statutory timescales. *MHRA-Performance-Metrics_CIT_2302-2401_CI_2303-2402.pdf (publishing.service.gov.uk)*
- More than half of all applications require additional information to be submitted before the application can be considered. The common issues have been published. *Common issues: Clinical - GOV.UK (www.gov.uk)*
- First approval via the new International Recognition Procedure has been granted. The product was authorised in 30 days providing UK patients with early access to this approved treatment. *MHRA grants first approval via the new International Recognition Procedure in 30 days - GOV.UK (www.gov.uk)*

US INITIATIVES & FDA GUIDELINES

FDA Centre for Drug Evaluation and Research (CDER)

CDER has launched a new 'Centre for Trial Innovation' for experts to discuss new methods for clinical trial design and conduct. *FDA launches new clinical trial center to improve innovation, communication | RAPS*

CDER's Accelerating Rare diseases Cures (ARC) Program provides a strategic overview of CDER's rare disease activities and expertise. *Accelerating Rare disease Cures (ARC) Program | FDA*

FDA Guidance Documents

During the COVID-19 pandemic, the FDA used legally available waivers to enable guidance documents to be issued without a public comments period.

In January 2024, the FDA issued a draft guidance proposing to continue this procedure for Level 1 guidance documents: *Background: FDA Good Guidance Practices | FDA*

The feedback received has however not been supportive. *Federal Register :: Food and Drug Administration's Draft Report and Plan on Best Practices for Guidance; Availability*

Final FDA Guidance Documents:

- February 2024: Charging for Investigational Drugs Under an IND *53685874fnlrv1_1.pdf (fda.gov)*
- February 2024: Assessing COVID-19-related symptoms in outpatient adult and adolescent subjects in clinical trials of drugs and biological products for COVID-19 prevention or treatment *55506416fnl_Assessing COVID-19-Related Symptoms.pdf (fda.gov)*
- March 2024: Artificial Intelligence and Medicinal Products – How CBER, CDER, CDRH, and OCP are Working Together *omp_aimedicalproducts_final_240313.pdf (fda.gov)*
- April 2024: Providing Regulatory Submissions in Electronic Format: IND Safety Reports *49868122fnl_IND Safety Reports.pdf (fda.gov)*

Draft FDA Guidance Documents:

- March 2024: Key Information and Facilitating Understanding in Informed Consent *10468178dft.pdf (fda.gov)*
- April 2024: Data Integrity for In Vivo Bioavailability and Bioequivalence Studies *46882322_dft_gui_draft_data_integrity_for_in_vivo_bioavailability_and_bioequivalence_studies_published.pdf (fda.gov)*

REAL-WORLD DATA (RWD) AND REAL-WORLD EVIDENCE (RWE)

DARWIN EU – Data Analysis and Real-World Interrogation Network

DARWIN EU will expand its capacity to deliver RWD studies. Since its launch in February 2022, 14 RWD studies have been completed and 11 are ongoing. The network currently operates with 20 institutions from 13 European countries. *DARWIN EU® continues expanding its capacity to deliver real-world data studies | European Medicines Agency (europa.eu)*

Catalogue of RWD Sources and Studies

On the 15 February 2024, the EMA and the Heads of Medicines Agencies (HMA) launched two electronic catalogues to help regulators, sponsors and researchers identify and use RWD when investigating the use, safety and effectiveness of medicines. *Multi-stakeholder webinar on the HMA-EMA Catalogues of real-world data sources and studies | European Medicines Agency (europa.eu)*

EMA Draft RWE Reflection Paper

The public consultation for 'Reflection paper on the use of real-world data in non-interventional studies to generate real-world evidence' is open until 31 August 2024. *reflection-paper-use-real-world-data-non-interventional-studies-generate-real-world-evidence_en.pdf (europa.eu)*

FDA Draft RWE Guidance

The FDA has issued a draft guidance 'Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products'. This guidance is one of a series of FDA's RWE Program documents. Comments are due by 18 June 2024. *55680653dft.pdf (fda.gov)*

POST PANDEMIC INITIATIVES

New Global Network for Coronaviruses

The World Health Organisation (WHO) has launched a new network to address the threat of coronaviruses, by coordinating global expertise and facilitating early and accurate detection of all coronaviruses of public health importance. *WHO launches CoViNet: a global network for coronaviruses*

COVID-19 Vaccine Strain Updates

Following a workshop organised by the International Coalition of Medicines Regulatory Authorities and the WHO, global regulators have agreed on timing and data requirements. Updates on vaccine composition have to be considered on a regular basis because protection from vaccines wanes over time as new variants emerge. *COVID-19 vaccine strain updates: Global regulators agree on timing and data requirements | European Medicines Agency (europa.eu)*

EMA's Emergency Task Force (ETF) has recommended updating COVID-19 vaccines to target new JN.1 variant. *ETF recommends updating COVID-19 vaccines to target new JN.1 variant | European Medicines Agency (europa.eu)*

Thank you for taking the time to read this Industry Update from S-cubed

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